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Attitude of Venereal Disease Patients Toward Clinics and Rapid Treatment Centers: During the latter part of 1947, questionnaires were developed for gathering information concerning the attitude of VD patients toward clinics and rapid treatment centers. Seven states participated in the study, sending in a total of 1,668 completed questionnaires by the end of 1948. Effort was made to insure confidence, no names were requested on the form, privacy was assured, and the form itself was given in a folded condition to the respondent upon leaving the clinic or center, being returned in most areas to a ballot box. The questionnaires were given to all treatment center patients and, in the clinics, to patients as well as persons who reported for diagnosis. All questionnaires distributed were actually completed, either by the patients themselves or by an interviewer in cases of illiteracy. There was no selection of patients; the findings can therefore be considered as representative, there being no biased selection of gripers or sampling errors.

The questionnaire, simple in design, was a single form involving 8 questions for use in the clinics and 6 for use in the treatment centers. Both forms requested not only background information (sex, race, and age), but also provided for the recording of any criticisms or complaints, the extent to which the item most criticized bothered the respondent, and an over-all appraisal of conditions. For those who might be hesitant to criticize, a loophole was provided by including a question concerning whether the respondent had heard any other persons complain about the clinic or center. The questionnaire thus provided for the recording of specific criticisms and certain background characteristics of the respondent, in addition to a measure of the patient's attitude.

Whereas the analysis of specific criticisms required only straightforward tabulation, the measurement of attitude involved the establishment of an attitude scale. For both clinic and treatment center questionnaires, 2 basic decisions had to be made regarding each question, (1) whether it contained components which reflected the respondent's attitude toward the clinic or treatment center, and (2) what type of question response best reflected this attitude. All questions considered as reflecting attitudes were cross-tabulated with each other. Coefficients of association were computed for each cross-tabulation and for all possible combinations of replies. Those questions and their particular response classifications which yielded relatively high coefficients of association were decided upon as reflecting, in combination, the attitude toward the clinic or center. The 5 questions thus selected formed a battery, each probing at the attitude from a different angle. These questions were combined to provide a single score, patients answering all 5 unfavorably were given a score of 5; those answering any 4 questions unfavorably were given a score of 4, and so on; those answering none unfavorably were scored 0. Fortunately, the same questions and responses could be used in scoring both clinic and treatment center questionnaires, thus permitting comparisons of the average scores between clinics, centers, and age groups.

The fact that reactions, on the whole, were quite favorable toward both clinics and rapid treatment centers affords much encouragement; however, certain internal comparisons of the data and the criticism tabulations may be of help in bettering the services.

The attitudes in the youngest age group, in both clinics and treatment centers, are about 4 times as unfavorable as attitudes in the oldest age group. This finding, important from a case-finding point of view, shows that everything possible should be done to insure good favor in the young age groups, because these young people, once served, may relapse or become reinfected; also, their attitudes may be passed on to contemporaries, the age group with high syphilis incidence. The fact that there were such large differences from clinic to clinic and among treatment centers indicates the possibility for improvement.

Unfavorable attitudes may have more bearing on the case-finding program than was thought possible. Of the 835 persons questioned at clinics, 8.5 percent said that they would not recommend the clinic to a person who needed an examination for venereal disease, and 4.1 percent of 833 persons questioned at treatment centers checked that they would not recommend the center to a person who needed treatment. At the clinics, persons were also questioned concerning whether they had ever recommended the clinic to anyone. The fact that 42 percent had so recommended the clinic indicates that recommendation in talk with others may be an important factor in the case-finding program.

Further evidence to indicate the importance of word-of-mouth advocacy of diagnostic facilities was shown in data resulting from the administration of another questionnaire to persons with primary and secondary syphilis in a treatment center. In contrasting the responses of patients brought to diagnosis through contact investigation or some required test (nonvolunteers) with those coming to diagnosis of their own accord (volunteers), it was seen that for both groups a large percentage had talked over their trouble or symptoms before their examination, relatively more of the volunteers having done so. Concerning the advice received, the volunteers tended to get better information, notwithstanding the fact that one out of the 65 who had talked with others was told, "Don't go to the clinic."

Two methods of improving the attitudes of those served by clinics and treatment centers exist, viz., (1) to propagandize, and (2) to take into account and to correct shortcomings which may have contributed to the formation of unfavorable opinions. Tables 4, 5, and 6 present in summary fashion the specific criticisms noted on the interview forms. Whereas some of the items may be corrected by direct attack, there are some which may require indirect action. For example, although further reduction of waiting time in a clinic may be financially impossible, even after a review of administrative procedure and physical set-up, the waiting time may be made to seem shorter by the provision of reading material, music, or educational movies, as is done in some clinics.

Table 4.—*Summary of criticisms of clinics and treatment centers*

	Clinics	Treatment centers
Number of patients filling out questionnaires	835	833
Number of patients listing criticisms	233	340
Number of criticisms	287	470
Number of criticisms per patient questioned	.34	.56
Persons mentioned in connection with criticisms (percent of total criticisms):	*Percent*	*Percent*
Physicians	7.0	1.1
Nurses	1.7	3.4
Medical students	3.5	
Investigators	.4	
General personnel	3.8	1.1
Other patients	.3	4.4
Total referring to persons	16.7	10.0
No person mentioned [1]	83.3	90.0
Total	100.0	100.0

[1] The form did not suggest that persons be mentioned in connection with the criticism. The tabulation is then that of free response.

Table 5.—*Criticisms of clinics*

	Percent distribution of 287 criticisms	
Handling of patients	37.3	
Wait in line too long		26.8
Personal attitude of some staff members		3.5
Mixing of sexes; mixing of races		2.8
Discourteous or unfriendly; rough		2.1
Not enough time given; tardiness in starting clinic session		2.1
Treatment	23.4	
Hurts (reference to needles or shots)		7.7
Hurts (no reference to needles or shots)		4.9
Takes too long		4.5
No good; poor or improper nursing or medical care		3.5
Make you come back		2.8
Conditions (physical and personal)	19.4	
Privacy in examining room		4.9
Unclean; location; comfort facilities		4.5
Understaffed		2.4
Organization		2.4
Give your name; people talk, meet people you know		2.4
Miscellaneous		2.8
Patient education:		
"They don't tell enough"	7.7	
Clinic hours:		
More night hours; more days open; not enough hours	7.7	
Posttreatment observation:		
Too long a period; not often enough; too often	2.8	
Diagnosis:		
Takes too long; poor or improper	1.7	
Total	100.0	

Table 6.—*Criticisms of rapid treatment centers*

	Percent distribution of 470 criticisms	
Food	29.0	
Treatment	20.8	
Hurts (reference to needles or shots)		10.4
Hurts (no reference to needles or shots)		6.0
Takes too long; poor or improper nursing or medical care		2.3
Type of treatment		1.9
Posttreatment observation too long		.2
Policies	16.2	
Visitor restrictions		4.5
Rules and regulations (or lack of them)		4.5
Patients working		3.8
Liberty		3.4
Handling of patients	6.8	
Personal attitude of staff		3.8
Mixing of races; mixing of sexes		2.1
Wait in line too long; rough		.9
Miscellaneous conditions (physical and personal)	27.2	
Reading facilities		5.1
Comfort facilities		3.9
Unclean		3.4
Noise; lack of rest		3.2
Bed linens		3.2
Organization or management		1.9
Other		6.5
Total	100.0	

These tabulations of criticisms, although representative only for the areas participating in this study, may be of value in pointing out conditions which generally bother persons who make use of clinics and treatment centers. Duplication of this type of study is unnecessary to determine what particular criticisms are prevalent in a particular clinic or center. Considerable information might be secured in areas in which there is an interest in patient relations by the use of a suggestion box which could be used by patients to vent their criticisms. A summary of such suggestions and/or criticisms, although not representative for a particular clinic or center, might provide useful information upon which action could be taken. (J. VD Information, Oct. '49, L. J. Usilton and J. W. Morse)

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Characteristics of the Cerebrospinal Fluid in Lymphogranuloma Venereum: In the course of treating patients with venereal diseases, it was noted by one of the authors, as has been noted by others, that there were abnormalities in the protein fraction of the cerebrospinal fluid in patients having lymphogranuloma venereum. The purpose of the present study was to evaluate these abnormalities with regard to their incidence, the possible mechanism of occurrence, and their diagnostic value.

The data were derived from case records in consecutive admissions of patients with lymphogranuloma venereum to the United States Public Health

Service Medical Center in Hot Springs National Park, Ark., beginning in January 1948. The diagnosis in all cases selected was made by or confirmed by a positive intradermal Frei test (using Lygranum antigen and showing greater than 9 mm. of induration and erythema). In many of the cases clinical evidence of the chronic form of the disease was present. Because other diseases coexisted in many patients, those records which revealed the presence of a condition which has been known to produce similar abnormalities in the cerebrospinal fluid were dropped from the study.

In the Hot Springs Medical Center, the cisternal fluid instead of the customary lumbar fluid of patients is routinely examined. Merritt and Fremont-Smith set the upper limit of normal for protein in a cisternal fluid as 25 mg. percent. Because the data on cisternal fluid have seldom been based on a large series of cases, the authors felt it advisable to offer as a control group 108 consecutive cases in which lymphogranuloma venereum was not present but collected by the same other criteria as the study cases. In these control cases the mean value of the total protein was 15.8 mg. percent, and in all but one the colloidal mastic reading was expressed as 00000. In 2 cases (1.85 percent) there was elevation of total protein beyond 24.0 mg. percent, and in one of these the fluid also gave a mastic reading of 10000. For purposes of this study a cisternal fluid was considered to be abnormal with regard to total protein if it showed greater than 24 mg. percent or colloidal mastic if it showed a positive reading in more than one tube.

In 19 (23.2 percent) of 82 cases of lymphogranuloma venereum, there were abnormalities in the cerebrospinal fluid, as contrasted to 2 (1.85 percent) in the control series of 108 cases. In each of the 19 cases there was at least one positive tube in the colloidal mastic, although the reading of 10000 when it occurred as an isolated finding was not included as an abnormality. It was further noted from the clinical signs in these cases that the patients were largely in the chronic stage of the disease, with some of them free from clinical evidence of lymphogranuloma venereum. In the total series of 82 cases no attempt could be made to break down the data by the stage of the disease. Because consecutive cases were chosen, however, some of the patients were in the early phase of their infection; these did not present abnormal cisternal fluids.

The literature shows that the virus causing lymphogranuloma venereum was first isolated in 1930. It was soon demonstrated that the virus diffuses rapidly through the body and produces granulomatous lesions in many different organs. One specific finding was that of hyperproteinemia accompanied by hyperglobulinemia. Many of the early workers believed this to be of definite diagnostic importance. This derangement of protein was found to be a permanent change, but no definite conclusions were made concerning whether this indicated persistent infection. In 1935, Saenz stated that recent experiments had proved an extraordinary affinity of the virus of lymphogranuloma venereum for the nervous system. Other workers showed that the inoculation into guinea pigs of the spinal

fluid from patients with lymphogranuloma venereum produced typical clinical and histopathological changes of the disease in 25 percent of the guinea pigs. Sabin has stated that the virus of lymphogranuloma venereum could be the cause of severe meningoencephalitis in man.

Observations of spinal fluid changes in this disease were not found in the American literature, and very few were uncovered in the foreign literature. In one article, published in 1939, complete spinal fluid studies in 6 of 8 cases were reported. All 6 showed abnormalities in the colloidal mastic curve comparable to those observed in the authors' study.

One explanation of the observed cerebrospinal fluid abnormalities is that they represent products of a local reaction, protective in nature, evoked by a low-grade meningoencephalitis resulting from viral invasion of the central nervous system. Conceivably, however, these abnormalities may represent spilling over into the cerebrospinal fluid of the increased serum protein noted by many observers. The fact that the changes are largely in the first zone of the colloidal mastic test is consistent with the hypothesis that the albumin/globulin ratio has been lowered. It will remain for electrophoretic or other fractionation studies to reveal the actual nature of the protein present.

This finding of increased cerebrospinal fluid protein, with consequent changes in the colloidal mastic test, may prove to be an aid to the physician's diagnostic armamentarium, and it may conceivably represent the only indication of activity. At present, there are no data to show that such findings are an indication of activity or that they are of prognostic significance. The presence of unexplained abnormalities in the protein or colloidal tests in the cerebrospinal fluid of a patient should suggest to the clinician the possibility of lymphogranuloma venereum and warrant a Frei test. More work is needed to evaluate both the mechanism and the precise nature of the protein changes which have been observed. (J. VD Information, Oct. '49, L. Finberg et al.)

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Chloramphenicol in Typhoid Fever: In a preliminary report, Woodward and his co-workers stated that chloramphenicol exerted a specific therapeutic effect in 10 patients with typhoid fever whom they treated in Malaya. In another group of patients with this disease, most of them treated in Mexico, McDermott, Knight and Ruiz-Sanchez observed that the administration of chloramphenicol was uniformly followed by prompt recovery, which, in most cases, was dramatic. These observations were somewhat in contrast to experiences reported with the administration of aureomycin in typhoid fever, the results of which have been irregular and, on the whole, rather unimpressive. When a supply of chloramphenicol became available, a study of its effects in typhoid fever was undertaken; the findings in the first 4 patients and in a typhoid carrier are reported below.

The first 3 patients were treated at the Massachusetts General Hospital. The fourth patient was treated on one of the medical wards of the Boston City Hospital, and the typhoid carrier was studied at the South Department of that hospital. Specimens of blood, stools, and urine were obtained before treatment and at intervals after treatment as indicated and feasible.

In the first case treatment was undertaken early in the third week of the disease with doses of 2 Gm. a day. Defervescence occurred by lysis between the third and ninth days of therapy, with steady symptomatic improvement over this period. Salmonella typhosa could no longer be obtained by culture from the blood or feces after the first day of therapy, and convalescence was uneventful. There were no untoward effects from the chloramphenicol.

In Case 2 treatment with daily doses of 4 Gm. of chloramphenicol was started at the end of the second week of illness. The patient continued to be acutely ill for about a week, and the temperature dropped progressively between the fifth and eighth days of treatment. S. typhosa bacillemia was demonstrated during the first 2 days of this therapy, but cultures of blood, urine and stools obtained after that time were all negative with the possible exception of the blood culture made on the second day after the treatment was stopped. Rather severe and persistent vomiting occurred during the first week of chloramphenicol administration, and may have been responsible for the delayed response in this patient.

In Case 3 there was a full-blown clinical and bacteriologic relapse after an apparently good response to an initial course of chloramphenicol that was begun in the middle of the second week of the disease and consisted of 43 Gm. given over a period of 13 days. After starting a second and more intensive course of chloramphenicol, improvement again followed quite promptly. There were no untoward effects from the first course, but the patient was nauseated throughout most of the second course and vomited several times soon after the larger dosage was started. This patient also experienced glossitis and cheilitis that may have been attributable, in part, to the antibiotic.

In Case 4 treatment with 6 Gm. of chloramphenicol daily was started during the middle of the fourth week of the disease, and the patient maintained for 2 full weeks on that dosage and for an additional week on 4 Gm. a day. She became and remained afebrile after the third day of this therapy, but she continued to shed S. typhosa in her stools throughout the period of treatment and the organisms were recovered again more than 3 months later. The effect of therapy on the symptoms was difficult to evaluate in this case. Distressing gastric symptoms accompanied the larger doses of the antibiotic, but were less marked and somewhat delayed during the second course when smaller doses were given.

In the chronic carrier (Case 5), the organisms could not be isolated from the stools during the 2 weeks of chloramphenicol therapy and for a brief period

thereafter. The organisms then reappeared in the stools and could be recovered quite regularly. This patient experienced mild diarrhea but no upper gastrointestinal symptoms while taking the antibiotic.

The strains of S. typhosa that were isolated from these patients and tested were found to be about equally sensitive to chloramphenicol. They were all partially inhibited in concentrations of 4 micrograms per cubic centimeter; some of them were completely inhibited in the same concentration, whereas others required twice that concentration for complete inhibition. All strains isolated from different sources and at different times from the same patient showed the same sensitivity to chloramphenicol. There was no tendency toward the development of increased resistance during treatment.

It is quite apparent from the results obtained in this small group of patients that chloramphenicol, although it may have had a beneficial effect on the course of the acute disease, did not produce the dramatic effects that were expected. The persistence of the organisms in the stools in Case 4 and in the carrier, the clinical and bacteriologic relapse in Case 3 and the rather slow defervescence in 3 of the 4 acute cases indicate that chloramphenicol, like aureomycin, still leaves much to be desired as a curative agent in typhoid fever. Relapses with bacteremia were also noted in 2 of the 10 chloramphenicol-treated patients reported from Malaya and were not uncommon after treatment with either chloramphenicol or aureomycin among the cases studied by McDermott, Knight and Ruiz-Sanchez. Serious complications, an intestinal hemorrhage in one case and perforation in another, occurred on the fourth and the second afebrile day, respectively, in 2 additional chloramphenicol-treated patients from Malaya.

The possibility that strain differences account for the variations in response to treatment was considered. Phage typings indicated that the strains from the acutely ill patients all belonged to the same type (E_1), whereas the carrier's strain was of a different type (A). Differences in response dependent on the host or on the nature of the lesion at the time treatment was started cannot be ruled out. With respect to the latter, McDermott et al. considered that aureomycin exerted an effect on the course of the infection particularly when treatment was started during the first 10 days of the disease. These effects were seldom dramatic, however, and in well established infections (third week) were frequently negligible. Chloramphenicol administration, by contrast, was uniformly followed by prompt and usually dramatic recovery in their experience. Although McDermott and his colleagues found chloramphenicol to be markedly superior to aureomycin as a therapeutic agent in typhoid fever, the authors own limited experience to date shows that, except for a lower incidence of gastric symptoms with chloramphenicol, the difference between the effects of these antibiotics has not been so striking. Diagnosis and initiation of treatment early in the disease and possibly the use of maximal doses from the start and continued for long periods may be determining factors in the success of both these agents in some cases.

The recent studies of Seligmann and Wassermann on the action of chloramphenicol on salmonella are of interest in relation to the findings in the present cases and particularly with respect to the failure to eliminate S. typhosa from the feces in Case 4 and in the chronic typhoid carrier. All of 23 salmonella types that these authors studied, including S. typhosa, were sensitive to 2 or 4 micrograms. However, in experimental infections with Salmonella typhimurium in mice, chloramphenicol failed to control the infection and exerted no influence on the intestinal flora when given orally or subcutaneously even in large doses and when treatment was started immediately after infection. (New England J. Med., 13 Oct. '49, H. S. Collins and M. Finland)

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Use of Diethylstilbestrol to Prevent Fetal Loss from Complications of Late Pregnancy: The results of stilbestrol therapy in 95 patients for the purpose of preventing complications of late pregnancy were reported upon previously; however, these 95 cases are included in the present study of a total of 180 women in whom the indication for therapy was diabetes, essential hypertension, nephritis or a past obstetric history of pre-eclampsia, eclampsia, premature delivery or unexplained intrauterine death of the fetus. The use of stilbestrol in pregnancy is based upon experimental evidence of its progesterone-stimulating effect in rats and in pregnant women. The authors were particularly interested in its possible value for the prevention of complications of late pregnancy, because a premature deficiency of the placenta in the secretion of estrogen and progesterone before and during late-pregnancy toxemia, premature delivery, and intrauterine death had been shown by the authors' studies and confirmed by others. The authors have emphasized the fact that, whatever the primary causes of these complications may be, a premature deficiency of estrogen and progesterone sooner or later is involved and becomes an intermediate contributing factor. The authors have also emphasized the reciprocal relation between vascular supply to the uterus and hormonal support, adequate vascularity being as essential for the normal production of the placental steroid hormones as adequate hormonal support is for the increased vascular demands of the pregnant uterus. The supplying of an extra stimulus for the secretion of estrogen and progesterone represents an attempt to combat only one of the contributory factors of the final syndrome. If a more normal secretion of estrogen and progesterone is accomplished, however, the vascular deficiency should be minimized, because the combined action of these 2 steroid hormones is characteristically one of vascular and myometrial growth. Experimental and clinical experience indicates that neither one of them alone could accomplish the degree of uterine growth and vascularity required in late pregnancy. Improved clinical results in themselves, therefore, would provide added support for the stimulative effect of stilbestrol upon the placental secretion of both the sex steroids.

From these considerations it is apparent that stilbestrol administration could not be expected completely to prevent late-pregnancy complications. By

combating one of the contributory factors in vascular deficiency, however, one might well postpone, if not entirely avert, the onset of the final clinical abnormality. This in itself would result in less damage to the mother and a greater chance for fetal survival.

Of the 180 pregnancies being reported upon, 104 patients were those of other obstetricians and the other 76 were patients referred to the authors at the Boston Lying-in Hospital, where the patients received their prenatal and obstetric care. All of the patients took stilbestrol by mouth according to the dosage schedule used in the authors' first study and which was as follows:

> In this dosage schedule which is based upon quantitative determinations of hormonal levels throughout normal pregnancy and is planned to approximate physiological conditions as closely as possible, 5 milligrams daily by mouth is started during the sixth or seventh week (counting from the start of the last menstrual period). The daily dosage is increased by 5 mg. at 2-week intervals to the fifteenth week when 25 mg. daily are being taken. Thereafter, the daily dosage is increased by 5 mg. at weekly intervals. Administration is discontinued at the end of the thirty-fifth week because a drop in estrogen and progesterone normally precedes the onset of labor. For the prevention of late pregnancy accidents stilbestrol is started as early as possible, but no later than from the sixteenth to nineteenth week, because a deficiency of estrogen oxidation products has been demonstrated during the second trimester in these patients. The initial dosage is always the one for the particular week of pregnancy when therapy is begun.

In no case was the therapy begun later than the nineteenth week and in the majority it was given from the start of the seventh to twelfth weeks. The authors do not recommend diethylstilbestrol except as a preventive measure for late-pregnancy toxemia. This statement is based on both theoretical grounds and actual experience.

All but 10 of the 180 women studied were multigravidas with a total of 380 previous pregnancies, only 7.5 percent of which had been normal. Fifteen percent of their previous pregnancies had terminated in spontaneous abortion. The other 78 percent had been complicated by spontaneous premature delivery, unexplained stillbirth or toxemia. Fifty women had pre-existing hypertension, either essential or secondary to renal disease. In the past obstetric histories of 105 pregnancies (no twins), there had been a 23 percent fetal loss from spontaneous abortion and a further 30 percent fetal loss from late-pregnancy accidents. On stilbestrol therapy there were 3 twin pregnancies making a total of 53 fetuses. Four of these (7.5 percent) were aborted, and another 4 (7.5 percent) lost after the period of viability. The factors operative in the reduction in fetal mortality during later pregnancy were a lowered incidence of superimposed toxemia and

of unexplained stillbirth and a decrease in fetal mortality in prematurely delivered infants.

Forty-nine patients had had a sequence of 3 or more consecutive pregnancies prior to stilbestrol therapy in which complications associated with progesterone deficiency had occurred. In at least 2 of the 3, abnormalities had developed after the period of viability. Only 3 percent of the previous 201 pregnancies had been normal, and only 27 percent of the offspring had survived. On stilbestrol therapy 61 percent of patients had no obstetric complications, and 85 percent gave birth to living children.

Sixty-six women had had pre-eclampsia or eclampsia in 94 of their previous pregnancies, with 41 fetal deaths, a mortality rate of 43 percent from this disease. According to Mastboom, 35 of these 66 women would have been expected to have toxemia in the pregnancy in which stilbestrol was given. Actually, only 14 of them had this complication with a 28 percent fetal mortality. Among the authors' records on 804 obstetric problem cases in which stilbestrol was administered there were 65 toxic pregnancies including these 14. The over-all fetal mortality from toxemia on stilbestrol therapy was 6.2 percent, as against 43 percent in the past obstetric histories of the same patients.

Seventy-six women had had spontaneous premature delivery in 83 percent of their pregnancies prior to the one in which stilbestrol was given. Forty-nine percent again delivered prematurely despite stilbestrol administration. The fetal loss, however, was reduced from 77 percent in the past obstetric histories to 20 percent on stilbestrol.

Analysis of the over-all data on the prematurely delivered infants of stilbestrol-treated mothers indicates that these babies are exceptionally heavy and long for their gestational ages and that, regardless of size, more of them survived than would have been expected from recent statistics on the mortality rates of premature infants. (New England J. Med., 13 Oct. '49, O. W. Smith and G. V. S. Smith)

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A New Concept of the Etiology of Hirschsprung's Disease: Recently, Swenson (one of the authors of this report) et al. have presented evidence supporting their contention that congenital megacolon is due to malfunction of the rectosigmoid that results in partial colonic obstruction. This obstruction accounts for the dilatation and hypertrophy of the colon, which retains peristaltic function. There is much evidence to support this concept of the etiology of congenital megacolon. The signs and symptoms of Hirschsprung's disease are those which ordinarily follow chronic, low, partial colonic obstruction. Distention,

audible and visible peristalsis, cramps and vomiting occur in varying degrees. Large fecal impactions are frequently present in the left side of the colon, whereas the rectal ampulla remains empty. Hirschsprung commented specifically on this finding in his paper. Patients are relieved by colostomy above the area of malfunction; within 3 or 4 months dilatation of the colon largely disappears, and hypertrophy diminishes. However, if the colostomy is closed the syndrome recurs, but reopening of the colostomy again provides relief.

Neuhauser was the first to demonstrate by roentgenograms and to attach significance to a narrow segment of rectosigmoid distal to the dilated sigmoid in Hirschsprung's disease. He described this for the first time 4 years ago and has subsequently demonstrated it in 40 patients with congenital megacolon. This lesion, which Neuhauser and the authors consider pathognomonic of Hirschsprung's disease, is at times difficult to demonstrate. It is recommended that only a small amount of barium be injected while the patient is being examined under the fluoroscope in an oblique position. One can then observe the narrow, irregular rectum and rectosigmoid distal to the markedly dilated sigmoid. These important changes in the rectum and rectosigmoid are missed if the lower colon is flooded with too much barium.

Resection of the rectum and rectosigmoid in 34 patients has resulted in one postoperative death and in what appears to be complete cure in the remaining 33 patients. This is accomplished by a special operative technic which preserves the anal sphincter. These patients have been followed for periods up to 2 years. Re-examination by barium enema has demonstrated return of the colon to approximately normal size and contour by the third postoperative month. More important, post-evacuation films show essentially normal emptying of the colon. Postoperatively, these patients are on normal diets and do not require laxatives, enemas, or drugs. In 3 patients the authors have demonstrated normal colonic peristalsis postoperatively by balloon studies.

The authors conducted a series of colonic-motility studies, using an apparatus patterned after that used by Chapman. It consisted of 3 ink-writing manometers, each attached by a long catheter to a balloon. Each balloon was filled with 10 cc. of air, and pressure changes were recorded on a kymorgraph. The authors have demonstrated in control patients that groups of strong peristaltic waves progress from the transverse colon to the anus. In 8 patients with Hirschsprung's disease strong peristaltic waves have been recorded in the dilated and hypertrophied colon. In 5 patients progression of the peristaltic waves along the enlarged segment was evident. In none of the 8 patients with Hirschsprung's disease did the peristalsis enter the narrow distal segment, which did exhibit increased tonus.

The authors believe that the absence of normal propulsive waves in the rectum and rectosigmoid constitutes a physiologic defect that results in chronic obstruction. This malfunctioning segment is identical with the narrow, irregular

bowel visualized by roentgenograms. There appears to be a correlation between the absence of ganglion cells in areas of the rectosigmoid and the physiologic defect. (New England J. Med., 13 Oct. '49, O. Swenson et al.)

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A Note on the Effectiveness of Treatment with Vitamin B_{12} in Tropical Sprue in Relapse: A short time ago, vitamin B_{12} was isolated and shown to have a profound effect on blood regeneration in persons with pernicious anemia, nutritional macrocytic anemia, tropical sprue and nontropical sprue. It also was found to be beneficial in relieving the acute and subacute combined degeneration of the spinal cord which so often is associated with pernicious anemia. However, until very recently the amounts of vitamin B_{12} available have been so small that investigators have not had sufficient amounts to treat patients fully. The authors decided to use part of their small supply of this material to make an intensive study of 3 patients with tropical sprue and to treat them over a considerable period of time, the thought being that it would probably take much larger amounts of vitamin B_{12} to produce full remission than might be apparent from the dramatic hemopoietic response produced by minute doses. The results in these 3 patients, who were studied in the hospital under controlled conditions, indicate that such is the case.

Repeated injections of crystalline vitamin B_{12} were given intramuscularly. Patient number one was given a total of 210 micrograms in 9 injections ranging in amounts from 10 to 25 micrograms in a period of 147 days. Patient number 2 received a total of 205 micrograms in 9 injections ranging in amounts from 10 to 25 micrograms in a period of 160 days. Patient number 3 was given a total of 200 micrograms in eight 25-microgram injections in a period of 138 days. In each case there was little or no detectable change for the first 3 or 4 days; then, when the reticulocytes began to rise in the peripheral blood on the fourth or fifth day, the patients began to feel better. Following the reticulocyte peak which occurred from the sixth to the ninth day the red blood cells and hemoglobin gradually increased. In each case there was gradual gain in strength, and in 2 of the patients who had diarrhea there was some improvement in their alimentary tract function although the stools did not become entirely normal.

No final conclusions concerning dosage and intervals between injections can yet be made but no therapeutic agent thus far used in the treatment of persons with tropical sprue has been so effective per unit of weight as vitamin B_{12}.

The case history for patient number one follows:

D.G., a 28-year-old Puerto Rican woman was admitted to the hospital in May 1948, complaining of loss of appetite, soreness of the tongue and diarrhea characterized by frequent, light-colored, foamy stools. She had been in good

health until after the birth of a normal child, 4 years prior to her admission. At this time she lost her appetite, had occasional nausea and vomiting and developed diarrhea consisting of from 6 to 8 soft, bulky, foamy, foul-smelling, light yellow stools daily. During the following 8 months she grew progressively weaker and lost 17 pounds in weight. At the end of this time she came to the Out-Patient Department of the hospital where a diagnosis of tropical sprue was made. She was given 8 cc. of crude liver extract 3 times a week. She improved only slightly and then, very slowly. She became discouraged and stopped coming for treatment. By April 1948 she again had developed loss of appetite, soreness of the tongue and severe foamy diarrhea. Within a month she was so weak that she came to the hospital and was admitted for treatment. Physical examination showed a poorly-developed, undernourished young woman who was obviously ill and chronically so. The mucous membranes were very pale. The tongue was smooth and red, especially at the tip and edges. Gastric analysis showed free hydrochloric acid in the gastric contents. The initial blood values were: red blood cells 2.41 million; hemoglobin 7.6 grams (48 percent); reticulocytes 1.0 percent. She was given a total of 210 micrograms of vitamin B_{12} in 9 injections in a period of 147 days. Fifteen days after the last injection her blood values were: red blood cells 4.12 million; hemoglobin 10.1 grams (71 percent); reticulocytes 0.8 percent. There was gradual clinical improvement. The soreness of the tongue and the diarrhea disappeared. When she was discharged after 166 days in the hospital she had gained 27 and 1/2 pounds in weight and felt able to work. (Blood, J. Hematol., Oct. '49, R. M. Suarez et al.)

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Freezing of Whole Blood: It is a generally accepted hypothesis that freezing and thawing of red cells results in hemolysis. Alternate freezing and thawing is a procedure commonly employed in the laboratory for the purpose of obtaining hemolysis. Preliminary experiments carried out in 1942 showed that the hypothesis is not correct under all conditions, i.e., it is possible to freeze whole blood in a solid mass and thaw it without appreciable hemolysis. Freezing of blood is here intended to mean solidification of blood by means of temperatures well below the freezing point of blood.

Early in this study, evidence showed that the type of water crystallization resulting from freezing was not an essential factor in the behavior of the red cells. Thus, equally good preservation of red cells was obtained by slow freezing at -3° C. or by very rapid freezing at -60° C. In the case of slow freezing, the mass of frozen blood showed formation of large crystals; whereas with fast freezing, the mass of frozen blood appeared very uniform. In fast freezing, one ml. of whole human blood collected in an acid-citrate-dextrose mixture was placed in a glass test tube and manually rotated in cracked CO_2 ice. Freezing occurred in a few seconds, and the tube containing the solid blood was removed instantly upon solidification and placed in the water bath at 37° C. to thaw with the aid of agitation. The hematocrit before freezing was 39.37; after freezing

and thawing, it was 39.07; the supernatant fluid showed no appreciable discoloration from hemoglobin. However, if frozen blood was allowed to remain in contact with CO_2 ice for even a few seconds after freezing, massive hemolysis resulted upon thawing.

Experiments on freezing of whole blood were resumed about a year ago. More than 150 specimens of blood have been frozen and thawed under varying conditions of temperature, heat dissipation (affecting the time of freezing), concentration of electrolytes, pH, concentration of diffusible and nondiffusible sugars (affecting the size of the erythrocytes), etc. In a series of a little over 100 specimens of blood, freezing and thawing were accomplished with a resulting hemolysis of less than one percent of the cells. Most of these specimens were collected in an acid citrate solution, with and without glucose. Even though freezing and thawing of red cells at -3° C. results in some hemolysis, the remaining red cells appear to be undamaged.

When whole citrated blood is placed in an air cabinet, cooled at -3° C, and allowed to remain undisturbed, it will remain liquid for an indefinite period of time. This has made possible the comparative study of blood preserved at -3° C. in the solid and in the liquid states.

The results obtained so far in the preservation of frozen and liquid blood at -3° C. are sufficiently encouraging to justify further studies, which are now under way.

Experiments have shown that regardless of the mode of freezing of blood, rapid thawing at +37° C. in the water bath with agitation is the best method to avoid hemolysis. Results similar to those reported for whole citrated blood may be expected, and have been obtained, with red cells suspended in various media. Much better results have been obtained when red cells are frozen after crenation produced by a hypertonic solution of sucrose, than when red cells are swollen by the addition of a hypotonic solution of glucose. (Science, 14 Oct. '49, M. M. Strumia)

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The Metabolic Fate of Infused Erythrocytes: In recent years, there has been considerable interest in the nutritional problems of surgical patients. In particular, nitrogen metabolism has been extensively studied, and it has become increasingly apparent that most seriously ill patients require amounts of nitrogen far above the needs of normal individuals. Most of these same patients receive many blood transfusions, and the question arises concerning to what extent these transfusions contribute to the patients' nutritional requirements. In particular, should the infused red cell nitrogen, which quantitatively is from 2 to 3 times greater than the associated plasma nitrogen, be included as intake in day to day balance studies?

The metabolic fate of infused erythrocytes in adults made significantly polycythemic by transfusions has not been known. Only inadequate and incomplete information has been available on erythrocyte survival and bone marrow function in such individuals. Data on these points were obtained in 2 normal adult males on a constant diet receiving serologically identifiable, fresh, separated erythrocytes. Observations were made on body weight, nitrogen balance, circulating plasma protein and erythrocyte mass, erythrocyte survival, serum bilirubin concentration, urobilinogen excretion, and liver function.

Plasma volumes, liver function, and circulating plasma proteins were essentially unchanged throughout the period of study. Survival time of the infused erythrocytes was not shortened. The infused red cell mass decreased at a normal, expected rate of 0.8 percent per day. Concomitantly, the mass of the recipient's own erythrocytes declined at a rate of from 0.4 to 0.8 percent per day in direct proportion to the relative amount of the infusions. This progressive fall in the subject's own erythrocyte mass was probably due to erythropoietic depression rather than to abnormally increased destruction. This is suggested by the normal survival of the infused erythrocytes and by urobilinogen excretion consistent with breakdown of the total red cell mass at a normal, not an increased, rate. There was a direct linear relationship between the extent of apparent bone marrow depression and the degree of induced polycythemia.

A slow, steady excretion of from 0.5 to 1.0 grams of nitrogen per day (above the control equilibrium value) began shortly after the infusions and continued for one month. The total extra nitrogen excreted was mathematically equivalent to 80 percent of nitrogen content of the infused erythrocytes. However, this excess nitrogen was derived only in small part from the infused red cells. The greater part could be accounted for almost completely by nitrogen diverted from normal erythrocyte synthesis as a result of apparent marrow depression.

The observations reported herein on the metabolic fate of infused erythrocytes in normal individuals should be extended to patients in both catabolic and anabolic diseases. At the moment, it would appear that the nitrogen of infused red cells should not be depended upon for contributing readily, quickly, or in great amount to the over-all nutritional requirements of the individual under stress. (Proj. C6-64-12-17, Rep. No. 64, 29 Sept. '49, Medical Nutrition Lab., Chicago, Ill., S. M. Levenson et al.)

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Hypersplenism: The once enigmatic, physiologically nonessential spleen has now fully proved itself to be an exceedingly unstable, and, therefore, pathologically important organ. Whether it has inherited, as a Mendelian dominant gene factor, the primary capacity to withhold and destroy excessive numbers of circulating red blood cells (congenital hemolytic icterus), or platelets (thrombocytopenic

purpura), or granulocytes (splenic neutropenia), or destroys all 3 indiscriminately at the same time (pan-hematopenia), - or, whether the spleen acquires these traits secondarily, through becoming involved in one or another of a number of unrelated constitutional diseases, - when the hypersplenic mechanism has been established by the appropriate diagnostic procedures now clinically available, quick and sure action by the surgeon is mandatory, and is usually effective.

As seen histologically, the spleen is not unique, presenting simply a reduplication of the cellular elements common to many other tissues and organs in the body. The lymph follicles are identical with those found in all lymph nodes. The reticulo-endothelial phagocytes, although greater in quantity, are not unlike in quality those found in liver, bone marrow, mesenteric lymph nodes, and the diffuse connective tissues. No specific secreting cells which would appear to be potentially capable of producing an internal secretion have ever been described. The specificity of the thrombocytopen of Trolland and Lee, and of splenin I and II of Ungar has as yet been difficult to confirm in other laboratories, including that of the author and co-workers. The experimental extirpation of the spleen in many animal species, and the accumulated experience of emergency splenectomy for traumatic rupture of the normal human spleen, have effectively confirmed these morphological findings and interpretations, and have firmly established the fact that this organ is not essential to the maintenance of normal health and longevity at any age in any species.

The Spleen and Its Vascular Sinuses. One must turn to anatomical considerations for at least a part of the explanation of the unique relationship which this organ seems to bear to the human pathological states. Unlike lymph nodes and liver, the spleen possesses a smooth-muscle-reinforced capsule and penetrating intraparenchymal trabeculae, which provide an intrinsic mechanism for the rhythmic physiologic contraction and relaxation of this organ. A sharp contraction of the spleen occurs after voluntary muscular exercise, after hemorrhage and after psychic (adrenalin) stimulation. The diagnostician may take advantage of this neuro-muscular mechanism to obtain a nonsurgical biopsy of the potentially mobilizable splenic cell content at any desired moment by securing peripheral blood cell and blood volume studies before and after the injection of adrenalin. A biphasic curve of total cell and differential fluctuations will reflect within from 30 to 90 minutes the initial contraction and subsequent compensatory hyperrelaxation of the spleen before it returns to its pre-adrenalin tonal equilibrium. By preceding such a study with sodium pentobarbital, it is possible to induce an initial relaxation of the muscular tone of the spleen with an increase in its sequestration of the blood elements reflected by a transitory reduction of as many as 37 percent of the circulating erythrocyte population.

From investigations carried out by various workers it would seem fair to accept as a current working hypothesis the concept that the human spleen has a

semi-open circulation, controlled by a filter mesh mechanism in the sinus wall, which by heredity or under many diverse pathologic conditions may be altered, either in the direction of greater or lesser selective permeability to the cellular elements of the blood. This circulatory mechanism, unique as compared with all other organs and tissues, operates to separate the cells from the plasma, and thus to concentrate in the spleen, both within and without the sinuses, in varying degree and quantity, blood cells of various types and quality. The more disturbed the circulatory equilibrium, the more profound and prolonged the stasis, the more does the spleen seem to lack discrimination and to withhold normal as well as fragile, senile and damaged elements.

The hypersplenic sequence of events may well include (a) abnormal stasis within splenic sinuses and/or pulp calling for a compensatory increase in delivery of marrow elements, (b) deplasmatization with increased mechanical intercellular friction, loss of erythrocyte potassium with other electrolyte disequilibria, leading to increased fragility, (c) pathologic concentration of lysolecithin and lysolecithin-like, spherocyte-inducing biochemicals normally produced in physiological amounts by the R-E cells, with hemolytic blocking or other polyhemagglutinin antibodies theoretically derivable from the R-E cells, exceptional opportunity for immediate contact-phagocytosis by R-E elements - all in all an ideal environment for the establishment of a vicious cycle of cell withholding and cell destruction capable of acceleration or deceleration, depending upon a variety of factors. The dramatic immediacy of the termination of a true hemoclastic crisis at the operating table, at the moment of ligation of the splenic pedicle, strongly incriminates this inherent, chemico-mechanical splenic mechanism.

The Role of the Bone Marrow. What role, if any, does the bone marrow play in the human hypersplenic states? The microcytic, spherocytic, hyperfragility of the erythrocytes associated with the hemolytic syndromes has been attributed to an inherited, inherent marrow defect. Dameshek and others have proved that all of these qualities are readily acquired by the definitive erythrocyte after marrow delivery, and it is difficult, if not impossible, to demonstrate these characteristics in the reticulocytes obtained directly from the marrow in these patients. The reports of a normal survival time for transfused erythrocytes from normal donors in patients with acute hemolytic crises, in contradistinction to a relatively shorter survival time for their own marrow product, and that such transfusion support should be given routinely, have not been confirmed in the experience of the author and co-workers. On the contrary, the author and co-workers believe the administration of borrowed red cells in acute hemolytic crises is both unnecessary and extremely dangerous. Attributing the excessive hemolysis of freshly transfused red blood cells in these patients to inaccurate isoagglutin or Rh typing, although this danger is always a possibility, can hardly account for all of the fatal reactions reported in the medical literature. Dameshek and Bloom also find this phenomenon to vary from case to case. In

one case of their recently reported series, the red cell survival time, studied by the Ashby technic, was diminished during crisis, and became normal only after splenectomy. These authors have failed to find instances of sudden acute pan-marrow aplasia, as reported recently by Owren in congenital hemolytic icterus, nor have the author and his co-workers encountered this particular mechanism in the true acute hypersplenic crises which have come under their observation in recent years. They have seen acute marrow aplasia, reflected by pancytopenia in the peripheral blood, but in each of these instances the differential diagnosis was established, first with reference to the exclusion of any hypersplenic factor, and then in terms of the type of specific infection, or chemical, or drug idiosyncrasy, individually or collectively responsible. It is entirely possible for hypersplenism and marrow aplasia to occur coincidentally in the same patient, or for aplasia to be precipitated in a patient with a previously demonstrated hypersplenic diathesis by any one of the many agents potentially operable in any other susceptible individual; but the author and co-workers believe the mechanisms should not and need not, be confused. If, and when, epidemic disease does attack several members in a family with an inherited hyperinstability of the spleen, it may more readily invoke a sudden transitory hypersplenic episode, but any direct bone marrow damage is an additional complication adding greatly to the hazards, in contrast with the excellent prognosis when the hypersplenic mechanism alone is involved.

Two other more probable marrow mechanisms, which may be mediated by or through the pathologic spleen, have been seriously considered and proposed, viz., cell maturation arrest and/or delivery inhibition or block. Krumbhaar many years ago showed a sustained supranormal rise in thrombocytes and erythrocytes in dogs post-splenectomy, suggesting some regulatory or inhibitory function affecting the level of circulating blood cells. Dameshek and associates have favored this interpretation of the cellular response which follows splenectomy in congenital hemolytic icterus, from studies of the fixed films and sections of marrow, and after finding no evidence of erythrophagocytosis in studies of the splenic histology, also in fixed sections. The author and co-workers' observations of fixed tissues in these cases have in every instance been supplemented by studies of the living marrow and spleen tissues, using supravital stains. Under these more favorable circumstances, it is quite easy to see, for example, in addition to those megakaryocytes rounded up in the resting phase, others in the same microscopic field with fragmenting cytoplasm in active platelet formation, even when a profound thrombocytopenia exists in the circulating blood. Likewise in aspirations or direct scrapings of living splenic tissue from any and all of the hypersplenic states, the highly phagocytic clasmatocytes or R-E cells are characteristically present in excessive numbers, at times from 10 to 12 per oil immersion field from a spleen weighing perhaps 2000 grams, differing only in the specificity of their phagocytized cell content, which in turn is directly related to the type and specificity of splenic reservoir cell sequestration, and is reciprocal to the circulating cytopenia. Specifically, in primary splenic neutropenia, the

bone marrow is hyperplastic for neutrophilic myelocytes which are obviously maturing normally with delivery of motile band forms into the circulation at an accelerated rate; the sinuses and parenchyma in the greatly enlarged spleen have their usual complement of sequestered mature erythrocytes almost entirely replaced by these same granulocytes which may be found both without and specifically within the highly phagocytic R-E cells; the capillary circulation meantime may show as few as 25 granulocytes per cu. mm.; adrenalin contraction of the spleen may be expected to raise this circulating increment of granulocytes transitorially to 10,000 or more per cu. mm., in which case, splenectomy is almost certain to correct the dyscrasia permanently.

From the foregoing discussion, the bone marrow mechanism, which the author and his co-workers have thought to be more frequently invoked in those pathologic states included in the definition of hypersplenism, comprises the following interrelationships: maximum compensatory hyperplasia, with normal maturation and accelerated delivery of the specific marrow element or elements involved, which elements, nevertheless, remain in dangerously low negative balance in the circulating blood because of an increasingly complete and absolute withdrawal of these essential blood cells by the spleen.

Final proof of the hypersequestration versus the marrow inhibitory role of the spleen in any given instance would seem to rest on the results of a carefully controlled study of the blood entering and leaving the spleen before and after adrenalin during surgical exploration in an active phase of such cellular disequilibrium. During the past year the author and co-workers have been making such observations in appropriately selected patients with the surgical cooperation of Dr. Robert Zollinger. These data will be presented in detail elsewhere. Suffice it to say, here, that this direct evidence effectively eliminates any bone marrow inadequacy of cell maturation and delivery as major factors, at least in those patients so studied, at the same time placing the full pathologic responsibility on the splenic tissue in situ.

In all but 5 of 49 consecutive cases of primary splenic thrombocytopenic purpura, there was an immediate and uniform increase in circulating platelets which occurred at the operating table on the day of surgery. Splenic artery and vein studies in a representative sampling of this series confirmed the bone marrow and adrenalin test interpretations of active platelet delivery; the splenic artery in one patient, for example, carried 450,000 platelets per cu. mm. to the spleen, although the vein leaving the spleen contained only 17,000 platelets per cu. mm. Five minutes after adrenalin injection into the splenic artery, the splenic vein contained more than 400,000 platelets. This could be interpreted either as a closing of the sinus-pulp reservoirs temporarily by the contraction of the spleen creating an arterio-venous shunt, or it could represent a reservoir release of temporarily trapped platelets; in either interpretation the integrity and activity of the bone marrow is attested. In 5 cases which showed a much

slower and more gradual postoperative increase in the circulating platelets, the evidence might be interpreted as a gradual recovery of inhibited megakaryocytes reciprocal to the gradual elimination of some humoral agent produced by the spleen. Lacking as yet objective reproducible evidence of a circulating thrombocytopen, this explanation must be left sub judice for the present.

In primary uncomplicated hypersplenism, then, as the author and co-workers have seen and interpreted these syndromes, the bone marrow plays only a reciprocal physiologic role, compensating, eventually maximally, in response to an excessive peripheral demand for blood cells, which demand fluctuates from time to time with the unpredicatability of an inherently unstable and pathologically hyperreactive spleen. The net increment of blood cells at any one moment in the circulating blood is always the resultant of the balance between supply and demand. Whenever any disturbance in this cellular equilibrium, so essential to health, occurs, either the supply must be increased or the demand reduced, promptly. In the hypersplenic states an excessive pathologic demand, more or less wholly created by the spleen, and which may or may not be compensable by the marrow must be eliminated. If and when the marrow becomes inadequate, the spleen must be promptly sacrificed, or the survival of the individual will be gravely threatened. Once freed of all splenic tissue, the author and co-workers have never found such individuals to show any further inadequacy or incompetence of the marrow for any and all demands through many years.

Primary Hypersplenism. Primary hypersplenism the author and co-workers define as an hyperinstability of the spleen, sometimes inherited as a Mendelian dominant gene factor, as in congenital hemolytic icterus, and, at other times, when direct human inheritance is difficult to establish, perhaps as a recessive character of infrequent expressivity. In such circumstances spontaneous hypersplenic episodes may occur, unrelated to any demonstrable internal or external environmental cause, such physiologic stresses as a normal pregnancy, and minor infections and traumas, frequently and repeatedly precipitate more or less severe hypersplenic exacerbations or crises in susceptible patients. For these reasons, whenever a true hypersplenism is recognized, prophylactic splenectomy must be seriously considered. Elective splenectomy is much to be preferred to emergency splenectomy. Irrespective, however, of the degree of cytopenia or of the acuteness of the clinical syndrome, the response to splenectomy is equally prompt and sustained. Furthermore, it is seldom that a pure hemolytic or an unadulterated thrombocytopenic or neutropenic syndrome is encountered. The predominant clinical picture may be anemia, with or without jaundice, or purpura, or Ludwig's angina and infection, but any one of these symptom complexes will be found more often than not to have a subclinical if not clinical cytopenia involving one or more of the other elements of marrow origin. At different stages in the clinical course of the same patient, differing degrees of pan-hematocytopenia may be observed reflecting the varying withholding idiosyncracy of the pathologic spleen for the cells coming to it.

One of the patients of the author and co-workers, a 14-year-old girl, when first seen in consultation, had a history of more or less continuous, severe pan-hematocytopenia since birth. Every laboratory examination showed every organic function to be normal, except for a pan-marrow hyperplasia of normally maturing cells in normal relative proportions, and for the adrenalin test which was interpreted as reflecting an unequivocal splenic pan-cellular hypersequestration. Splenectomy was followed by a prompt peripheral hematologic re-equilibration, and by a complete clinical metamorphosis from chronic invalidism to normal health and physical activity. The surgery was performed in October 1943. No other evidences of pathology have developed in the intervening 5 and 1/2 years.

Hypersplenism Secondary to Other Diseases. During the course of a number of diseases the spleen may become secondarily involved. In a certain proportion of these cases there develops a syndrome identical with one or another of those already described as primary hypersplenism, in which both specific splenic hypersequestration and compensatory bone marrow hyperplasia may be demonstrated, although there is no familial history of such a trait. Hemoclastic crises may occur which threaten the survival of the individual quite independently of his basic disease. Under such circumstances splenectomy is indicated and may, and sometimes must, be undertaken, with the more remote prognosis, however, correspondingly guarded. In no instance has any exacerbation of the underlying disease process been noted because of the splenic surgery, and most often the improvement which follows the re-establishment of a more nearly normal blood cell equilibrium is directly beneficial in the further management of the original disease.

In the author and co-workers' series of 326 splenectomies, the diagnosis in 270 cases was hypersplenism, and of the 270 splenectomies for hypersplenism, 176 (65 percent) have been classified as without otherwise demonstrable disease, therefore as primary, and 94 (35 percent) as secondary to some other obvious basic pathological process. Because of the frequency with which the spleen, when involved in other pathologic processes, has been observed to assume an aggressive activity against the blood cells entering its sinuses, it now seems appropriate to consider this organ as possessing a considerable degree of normal instability, not unlike, qualitatively, the inherited abnormal hyperinstability of the primary syndromes. The unique structure of this organ, as required for its physiologic functions, lends itself admirably to circulatory distrubances associated with parenchymal cellular invasion, and the large complement of phagocytic cells already there await only the time and opportunity which stasis and engorgement inevitably provide. Three examples only will be cited from this series. During the course of chronic lymphatic leukemia in a white male, aged 57, who had been under satisfactory control with radioactive phosphorus for several years, there developed an acute hemolytic crisis. Appropriate laboratory studies ruled out both radiation damage and lymphocytic myelophthisis of

the marrow as contributing factors although revealing a marked compensatory normoblastic hyperplasia, and splenic hypererythro-sequestration. Splenectomy was advised, after transfusions had proven ineffective and was followed by an immediate cessation of erythrocyte destruction. The underlying leukemia has continued to respond to small infrequent doses of radioactive P-32 to the present time. There have been no further hemolytic episodes. A white male patient aged 39 years presented all of the clinical and hematologic findings characteristic of acute primary thrombocytopenic purpura, including typical compensatory megakaryocytosis in the bone marrow without other demonstrable pathology. Splenectomy was followed by an immediate and sustained thrombocytosis, and the prompt disappearance of all purpuric manifestations. Histologic study of the spleen, however, revealed a well developed Hodgkin's granuloma, although neither liver nor lymph nodes, grossly or microscopically, showed any sign of this disease at this time. One year later the primary disease proved terminal, despite intensive therapy, but there was no recurrence of the purpura which had threatened survival from hemorrhage a year earlier. A young woman, aged 20 years, whose sister 8 years previously had undergone splenectomy for Gaucher's disease, suddenly developed a rapidly enlarging abdominal tumor associated with profound peripheral blood changes. The total circulating leukocytes were only 1300 per cu. mm., the red cells 3,180,000, and the platelets 111,440. An adrenalin test decreased the tumor size and increased temporarily the circulating level of all of the normal blood elements. A sternal marrow study showed compensatory pan-marrow hyperplasia of all essential elements. An occasional Gaucher cell was found which served to establish the diagnosis. Similar studies of the sister's marrow revealed Gaucher cells in limited number, insufficient, however, to have influenced adversely the normal circulating blood cell equilibrium during the years since her earlier splenectomy. A 5000 gram spleen was removed without complications, followed immediately by the re-establishment of a normal sustained circulating level of all blood cells. Marriage and a normal pregnancy have been accomplished without untoward incident meantime.

The table on the opposite page shows the range of diseases thus far encountered in the author and co-workers' clinic, which have shown at some time during their clinical course, an involvement of the spleen sufficient to precipate a more or less acute hypersplenic crisis, for which complication, surgery has been deemed imperative for survival. In none of these individuals has it been possible by history or direct examination of blood relatives to establish an hereditary factor. It is for this reason that the author and co-workers are hypothesizing a so-called normal instability of the spleen in its reservoir function for any or all of the blood cells, which due to the unique circulatory mechanism of this organ, plus its high content of R-E cell phagocytes, permits of ready imbalance in the circulating levels of the blood elements, which normally pass through or remain only temporarily in its parenchyma.

Acute Hemoclastic Crisis. As already stated, the hypersplenic mechanism, whether primary or secondary, may precipitate some of the most acute critical

1932 - 1949

270 SPLENECTOMIES FOR HYPERSPLENISM

PRIMARY

Congenital Hemolytic Icterus	75
Thrombocytopenic Purpura	77
Splenic Neutropenia	13
Splenic Pan Hematopenia	11

Recurrences

a. Accessory Spleens	4
b. Generalized R.E. Cell Hyperphagocytosis	5

SECONDARY

a. *Congestive Splenomegaly*

Banti's Syndrome	42
Felty's Syndrome	6
Acquired Hemolytic Icterus	16

b. *Infiltrative Splenomegaly*

Gaucher's Disease	4
Xanthomatosis	1

c. *Hemoblastic Splenomegaly*

Lymphatic Leukemia	4
Myelogenous Leukemia	2
Monocytic Leukemia	1

d. *Inflammatory Splenomegalies*

Tuberculosis	3
Syphilis	1
Moniliasis	1
Boeck's Sarcoid	2
Hodgkin's Syndrome	5

e. *Neoplastic Splenomegaly*

Retothelio Sarcoma	1
Hemangioma	2
Multiple Myeloma	1

f. *Myelofibrosis* with fibrous splenomegaly without myeloid metaplasia 2

(With myeloid metaplasia 4 cases, no splenectomy)

acellular clinical syndromes which the physician and surgeon are called upon to diagnose and treat. Uncontrollable hemorrhage, a profound hemolytic anemia, or sudden sepsis may dominate the clinical picture. An immediate and thoroughly critical blood and bone marrow study is the first essential in the differential diagnosis. There may be insufficient time for a confirmatory adrenalin test or other extensive laboratory investigations. The theoretical considerations, which may explain this sudden negative balance between bone marrow supply and peripheral demand for any or all of the essential blood elements, the author and co-workers believe involve both the mechanical and/or humoral factors inherent in the vascular and cellular organization of the spleen. Whether the blood platelets, the erythrocytes, the granulocytes, or any possible combination of these elements are found to be deficient in the blood stream, the marrow must be hyperplastic for their precursors, without evidence of maturation arrest or qualitative abnormalities, if and when a true uncomplicated hypersplenism is the sole cause. In such syndromes, splenectomy is followed by a prompt and complete cellular re-equilibration, as reflected in the 7 patients with acute erythroclastic crises in congenital hemolytic icterus and in the one patient with acute thrombocytopenic purpura. The curve of recovery of the red blood cells in each of these 8 cases follows the same general pattern and timing, although the anemia in the first 7 was hemolytic in origin and in the eighth it was secondary to hemorrhage. All of the factors which govern the specificity and degree of cellular deficit from patient to patient, and in the same patient from time to time are still unrevealed, but the evidence to date tends to incriminate the spleen rather than the bone marrow.

Relative Hypersplenism. In certain patients, who have experienced permanent marrow damage from industrial toxins, but in whom progressive mesenchymal destruction has been halted by removal from the environment, the normal physiologic reservoir function of the spleen may be sufficient to prevent cellular decompensation. After a sufficient period of supportive therapy, if the marrow hyperplasia continues to prove inadequate for the demand, splenectomy should be considered and will permit at times in selected patients, a more nearly normal circulating increment of cells.

Traumatic Rupture of the Spleen. Control studies have been made in those healthy individuals who have suffered sudden traumatic rupture of the spleen requiring emergency splenectomy for intra-abdominal hemorrhage and shock. In a survey of some 22 such individuals, the hematologic equilibria and the health and clinical resistance to ordinary infections have remained unimpaired. The normal human spleen is apparently not essential to life or good health. Conversely the pathologic human spleen may threaten both health and longevity.

Post-Splenectomy Failures and Recurrences. The importance of differential diagnosis in the establishment of a true hypersplenic syndrome cannot be overemphasized. Obviously other mechanisms may simulate superficially these specific splenic entities, the most common of which involve the bone marrow, upon the integrity of which the body is dependent for its continuing resupply of new cells throughout life. Progressive marrow hypoplasia on the basis of any nutritional deficiency or toxic agent, intrinsic or extrinsic in origin, must be recognized and corrected per se at the earliest possible moment. Myelofibrosis and osteopetrosis may be accompanied by compensating extramedullary hematopoietic splenomegaly, which when associated with a precipitated hypersplenic episode may strongly suggest splenectomy. Under such circumstances a positive adrenalin test will usually reflect a sharp increase in circulating nucleated red blood cells and myelocytes, but on occasion such evidence of local splenic hematopoiesis is lacking. If repeated bone marrow aspirations fail to reveal active blood cell regeneration from any and all sites (sternum, spinous process, iliac crest, ribs), it may be necessary to aspirate the splenic parenchyma directly, or secure a tissue biopsy, before a judgment may be reached concerning the relative importance of the productive versus the destructive roles of the spleen in any particular instance. In 6 such patients only 2 showed a predominant hyperdestructive activity by the enlarged spleen with negligible hematopoietic function. Both of these patients benefited by splenectomy. A tightly packed avascular leukemic marrow may simulate at times a hypoplastic state, and with a sub-leukemic peripheral absolute leukopenia, anemia and thrombocytopenia, may lead to an erroneous interpretation of the splenomegaly.

In only a very few instances, fortunately, have the author and co-workers encountered a generalized R-E cell hyperplasia and hyperphagocytosis, in nonbone

marrow cytopenic states, so that liver, lymph nodes, marrow and connective tissues participated sufficiently to render clinically ineffective the removal of the excessively large increment of phagocytes in the spleen. Until proven otherwise, therefore, the principal pathologic focus in these patients may be assumed to be the spleen.

Accessory Spleens. An initial characteristic post-splenectomy remission may at times be followed after a few months or even after several years by a recurrence of the same or an entirely different type of hypersplenic syndrome. Experience has taught the author and co-workers to be immediately suspicious of some remaining accessory splenic tissue when this occurs. The marrow is again studied immediately and must show specific hyperplasia of the deficient circulating elements without maturation arrest or abnormal qualitative alterations. Accessory spleens or implanted fragments of spleen from a traumatically ruptured or surgically torn spleen may become hypertrophied and functionally pathologic. Re-exploration is definitely indicated when the laboratory data confirm a recurrent mechanism of hypersequestration and destruction. Thorotrast visualization will frequently assist the surgeon in locating the embryonic splenic rests in remote areas, including the retroperitoneal gutter.

The first patient in this series to be subjected to splenectomy during an acute erythroblastic crisis in congenital hemolytic jaundice experienced a dramatic recovery hematologically and clinically, which lasted 4 and 1/2 years. At the end of this period the same type of hemolytic, icteric anemia re-appeared with reticulocytosis and compensatory normoblastic marrow hyperplasia identical with the first episode. When all medical measures had failed, a surgical re-exploration was undertaken and 3 small accessory spleens, totaling not over 5 Gm. by weight in all, were found and removed. Mesenteric nodes and a biopsy of the liver were obtained at the same time from normal appearing tissues, and histologic examination confirmed the normal state of these organs. The accessory splenic tissues, however, contained excessive numbers of highly phagocytic clasmatocytes loaded with red blood cells, and a second remission followed their removal. This has continued to the present time 11 years later, 16 years after the first operation.

The fact that few carefully studied hypersplenic episodes represent a pure single cell strain sequestration has been previously emphasized, together with the observation that the same individual patient may at different times show different cell-type deficits, reflected by entirely different clinical syndromes, all of which tends to center attention upon splenic tissue, its unique circulatory system, functionally designed for storing normal cells and salvaging damaged and senile blood elements, rather than upon the organ of their origin, the bone marrow. This double danger of differential splenic selectivity was demonstrated in one of the author and co-workers' patients in 2 dramatic episodes separated in time by 18 months. A young man 16 years of age developed without previous warning, an acute erythroclastic crisis, typical of congenital hemolytic jaundice.

Complete recovery followed splenectomy. Some 18 months later he developed, equally suddenly, an acute spontaneous fulminant thrombocytopenic purpura without any evidence of hemolytic anemia. Bone marrow studies confirmed the presence of increased numbers of actively multiplying and fragmenting megakaryocytes apparently responding to an increased peripheral demand for platelets. All other laboratory data excluded any other possible contributing mechanism. Following preoperative blood transfusions, a re-exploration was made and a 5 Gm. accessory spleen was discovered at the upper pole of the left kidney retroperitoneally. Upon its removal there was an immediate cessation of oozing in the operative field and the studies of the blood showed a coincident re-appearance of platelets in large numbers. There has been no further cellular disequilibrium in this patient to date.

Reference is made in this general connection to the patient already cited, who was first presented with a relatively pure primary splenic neutropenia, only to develop within 12 months a splenic panhematopenia involving all of the circulating blood elements, with complete and permanent pan-cellular re-equilibration following splenectomy, continuing 11 years to date.

Failure of complete and permanent restoration of health following splenectomy in true hypersplenic states will only be encountered in those individuals in whom the hypersplenism is secondary to progressive constitutional disease involving other organs. The ultimate outcome in such patients obviously will depend upon the effectiveness of the therapy for the primary disease. Nevertheless, when the predominant clinical syndrome in such patients can be proven to reflect an hypersplenic mechanism, this complication may and must be considered on its own merits. The best clinical judgment in the author's clinic has been more frequently than not to eliminate the focus of disease in the spleen together with the accompanying and resultant hypersplenic cellular imbalance, both of which threaten the health and survival of the patient. Only if a substantial cellular contribution is actually being made by a compensating, ectopic hematopoietic focus in the spleen, will the patient be less well off without rather than with his spleen.

Contraindications to Splenectomy. The contraindications to splenectomy may be sharply defined and clearly stated as (1) any acute or chronic bone marrow damage, (2) myelofibrosis, and (3) osteopetrosis in which the splenomegaly usually reflects ectopic hematopoiesis, (4) pan-myelophthisis, (5) ectopic splenic hematopoiesis plus secondary hypersplenism. (Bull. N. Y. Acad. Med., Oct. '49, C. A. Doan)

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Aureomycin in Molluscum Contagiosum: Experimental work of Wile and Kingery on the etiology of molluscum contagiosum led them to conclude that the disease is due to a filtrable virus. Further reports on the value of aureomycin

in diseases of the rickettsia-virus group led the authors to try it on a widespread case of molluscum contagiosum.

C. S. presented himself with a generalized eruption of molluscum contagiosum with approximately 300 lesions on the trunk and extremities. There was a history of the appearance of a dozen or so lesions on the trunk at first, and of the condition's becoming generalized a few days after a massage in a Turkish bath. A few of the lesions were curetted for diagnostic purposes.

Aureomycin was prescribed in doses of 250 mg. twice a day by mouth for 2 days. Four days after treatment with the drug had been stopped, the lesions were almost flat. No more aureomycin was prescribed, but white lotion N.F. was prescribed to be applied locally to hasten the removal of the remaining debris in the lesions. In another week nothing was left of the lesions but pigmented macules, and in the following week there was no sign of recurrence.

This dramatic response, although in only a single case, seemed to justify calling attention to the possibility of using this drug in molluscum contagiosum and in other conditions presumably of virus origin, such as verruca vulgaris, juvenile flat warts and plantar warts. (Arch. Dermat. and Syph., Oct. '49, W. H. Guy et al.)

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Course in Otorhinolaryngology, Oesophagoscopy, and Bronchoscopy: The Bureau of Medicine and Surgery announces a two weeks' course of instruction covering otorhinolaryngology, oesophagoscopy, and bronchoscopy given at the Georgetown University Medical Center, Washington, D. C., under the direction of Professor Georges Portmann of the University of Bordeaux, France. The inclusive dates of the course are from Monday, 17 April 1950 through Saturday, 29 April 1950. Although this course is of brief duration, it is highly endorsed and thoroughly covers the most salient factors pertinent to these specialties.

Requests for this course are desired from medical officers of the regular Navy and must be received in BuMed by 1 March 1950 in order to receive consideration.

The tuition fee will be borne by BuMed. Authorization orders ONLY will be furnished in accordance with Joint Letter 49-412 of Navy Department Bulletin dated 31 May 1949 and no reliefs will be provided for medical officers authorized to attend. (Professional Div., BuMed)

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Advance Study for Prospective Students at Naval School of Hospital Administration: In view of the fact that students recently undergoing instruction at the Naval School of Hospital Administration have had difficulty in assimilat-

ing the material presented in the accounting course, it is suggested that all prospective students of this school complete USAFI course No. FM-767, Accounting Principles, Volume 1, prior to reporting for instruction. (Personnel Div., BuMed)

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Course in Medical Aspects of Radiological Defense: Announcement has been made by the Atomic Energy Commission of a course in the Medical Aspects of Radiological Defense to be given at Rice Institute, Houston, Texas. The didactic training period will commence 2 February 1950 and will be 5 months in duration. This phase of the instruction will be followed by on-the-job training for 3 months at the Institute of Nuclear Studies, Oak Ridge, Tennessee.

Requests are desired immediately from medical officers of the regular Navy who are interested in this field of study. Each request must contain a 3-year service agreement. Requests may be made by dispatch if the time element involved requires such action. Dispatch requests must be confirmed by a following letter. (Professional Div., BuMed)

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Courses in the Technics of Using Radio-Isotopes in Research: The Bureau of Medicine and Surgery is in receipt of an announcement from the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee, setting forth the schedule for the next 3 sessions of the basic course in the Technics of Using Radio-Isotopes in Research.

The convening dates are 2 January 1950, 30 January 1950, and 6 March 1950. Each session is 4 weeks in duration. The tuition fee of $25.00 per officer will be borne by BuMed and authorization orders ONLY will be provided for those in attendance, in accordance with Joint Letter 49-412 of Navy Department Bulletin dated 31 May 1949. No reliefs will be furnished for attending medical officers.

Requests are desired from medical officers interested in this course of study and should reach BuMed as early as possible in order that final arrangements with the Oak Ridge Institute of Nuclear Studies may be completed prior to the convening date of each session. (Professional Div., BuMed)

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BUMED CIRCULAR LETTER 49-135 13 October 1949

To: Commandants, All Continental Naval Districts and River Commands

Subj: Contacts of Early Syphilis Cases; Telegraphic Reporting of (Report Symbol Med-060)

Refs: (a) NavMed P-1288, Interviewer's Aid for VD Contact Investigation, pp. 25-30.
(b) M.M.D., paragraphs 12B6.2 and 5120.

Encls: 1. (HW) List of State Health Officers
2. (HW) Government Identification Western Union Credit Cards

1. In order to expedite venereal disease contact investigation, the U. S. Public Health Service has arranged with the Western Union Telegraph Company for telegraphic reporting of early syphilis contact information between the States, Hawaii, Alaska, Puerto Rico, and the Virgin Islands. By agreement this service will include contact information from military installations as well as reports from civilian sources. Overseas activities and ships will be notified at a later date should this type of reporting be considered feasible for their use.

2. The plan outlined hereinafter is only applicable to cases reported by medical officers at naval and Marine Corps activities in the continental United States. Accordingly, the plan and method of reporting cases will be operated as follows:

(a) The U. S. Public Health Service has entered into a national contract with Western Union Telegraph Company to reimburse the Company for transmitting early syphilis contact information by telegram only when it meets the following conditions:

1. They are contacts reported by a patient with early syphilis.
2. The full name and address of the contacts are included in the wire.
3. The contacts live outside the State from which the report originates.
4. The contacts are civilians.

(b) All local civilian health officers and senior medical officers of naval and Marine Corps activities will be issued Western Union credit cards bearing the Public Health Service account number 244 and authorizing them to initiate telegrams for transmission to the State Health Department of the State in which the contact may live. Ordinarily these telegrams will be used only if at least one day can be saved in transmission in comparison with the usual means of communication. Night letter telegrams should be used whenever such service will not reduce the speed of the message transmission.

(c) Western Union offices in State capitols receiving such reports will re-route the messages to the appropriate local health authority in accordance with instructions obtained from the State Health Departments. This will ordinarily save at least one day over the usual time required for re-routing of contact reports mailed to State health officers.

(d) The Western Union Telegraph Company will bill the U. S. Public Health Service at the end of each month for the cost of messages transmitted during the preceding period.

(e) The telegram shall be addressed to one of the State Health Officers shown on Enclosure (1). The first portion of the message text shall consist of a code symbol giving the diagnostic classification of the patient - S10 for primary syphilis - S20 for secondary syphilis, and S30 for early latent syphilis, followed by the name of the contact, address, and other identifying information; e.g.,

"DR J P WARD
SUPERINTENDENT OF HEALTH
STATE DEPARTMENT OF HEALTH
PHOENIX ARIZ

S10 MARY JANE WILLIAMS 2917 ROSEMONT AVENUE

PHOENIX ARIZ WHITE AGE 21 WORKS AT NITE LIFE

CAFE

s/ SMO NAS
CORPUS CHRISTI TEX"

(f) All measages shall be telephoned to the closest commercial Western Union office unless other arrangements for Western Union to pick up messages have been made. The operator should be informed of the credit number and that the telegram is chargeable to the U. S. Public Health Service. In no instance shall the message be placed with naval communications unless for immediate releasing over the local Navy - Western Union tie line. In all instances it must be made clear that the telegram is chargeable to U. S. Public Health Service credit number 244.

(g) In addition to telegraphic reporting of contacts of early syphilis, the usual Venereal Disease Contact Reports (NavMed 171) shall be prepared and forwarded at the earliest possible date, including under "remarks". . . . . "Previously reported by telegram on (insert date) ."

3. Enclosed herewith are the Western Union credit cards prepared for your office and major naval and Marine Corps activities within the geographical limits of

your command. It is requested that specific instructions, including proper method of custody and use of the credit cards, be issued each senior medical officer along with each credit card.

4. It is requested that activities not issued a Western Union credit card be directed to forward contact reports as heretofore to the District Medical Officer's office who will release dispatches over his own credit card authorization, if the contact information meets the conditions enumerated in paragraph 2(a), and if one or more days in initiating contact investigation may be saved.

5. For contact reports of other venereal disease cases (including early syphilis contact information) not meeting the conditions set forth in paragraph 2(a), and use of air mail should be considered where at least one day can be saved over transmission by ordinary mail.

6. This procedure for telegraphic reporting of venereal disease contact information is considered to be in keeping with the confidential nature of the report.

--BuMed. C. A. Swanson

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BUMED CIRCULAR LETTER 49-136 18 October 1949

From: Chief, Bureau of Medicine and Surgery
To: All Holders of the Manual of the Medical Department

Subj: Advance Change 3-16, MMD

Encl: (1) Subject Change

1. The enclosed Advance Change 3-16 is effective immediately. It shall be recorded on the "Record of Changes" page in the Manual. The individual paragraph changes are to be inserted in their proper places in the Manual text.

C. A. Swanson

Note: This letter together with enclosures will be distributed as soon as the enclosures are received from the printer.

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BUMED CIRCULAR LETTER 49-137 Joint Letter 18 October 1949

From: Chief, Bureau of Medicine and Surgery
Chief, Bureau of Supplies and Accounts
To: All Ships and Stations

Subj: Improper Use of Insecticide Aerosol Dispensers

1. It has been reported that insecticide aerosol dispensers, which were designed primarily for indoor mosquito control, are being used for the control of flies, cockroaches, and other insects against which it has no lethal action in practical dosages. Unless stopped, these improper uses will cost the Navy thousands of dollars annually.

2. The greater portion of aerosol one-pound dispensers presently on hand are filled with the original pyrethrum-sesame oil insecticide intended solely for mosquito control. These stocks were procured during the war years. New Navy Department Specifications 51-D-15 dated 1 March 1946 and 51-I-5 dated 15 February 1949 incorporate DDT in the dispenser aerosol formula. Since all post-war procurement of aerosol has been limited to the DDT formula in forty-pound charging cylinders, it is believed that all one-pound dispensers that have been recharged from charging cylinders contain the DDT aerosol.

3. The pyrethrum-sesame oil formula without DDT is ineffective for use against practically all insects other than mosquitoes. It will knock flies down, but in ordinary dosages they recover. It will not kill hard-shell insects, such as beetles and cockroaches. Each dispenser is clearly labelled with the statement "Do not use for flies or insects other than mosquitoes." The DDT formula will kill flies as well as mosquitoes, but it is not to be used out of doors at any time, or indoors for any but these two insects, and even there it is not the preferred insecticide for flies.

4. The one-pound dispenser contains sufficient material to treat 150,000 cubic feet of confined space (4 seconds spraying for each 1,000 cubic feet or 8 seconds for the standard pyramidal tent). The use of aerosol dispensers should be supplemented by residual DDT sprays applied to bulkheads, overheads and screens. Where a space spray against flies or mosquitoes is required, the use of the pest exterminator spray gun, General Stores Section, Catalog of Navy Material, Stock Number 41-S-4112, with a Standard Navy Insecticide Stock Number 51-I-165 will be found to be satisfactory, and more economical than aerosol dispensers. One gallon of this insecticide costs approximately the same as one pound of aerosol and used carefully on a daily basis will be sufficient for several weeks, depending on the size of the area to be treated.

5. Where indicated, more rigid control should be exercised by local requiring activities in order to limit the use of aerosol dispensers to the elimination of mosquitoes in enclosed spaces. C. A. Swanson - C. W. Fox

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BUMED CIRCULAR LETTER 49-138 21 October 1949

From: Chief, Bureau of Medicine and Surgery
To: All Naval Hospitals and All Stations Having a Representative of the Medical Department Aboard

Subj: Standard Medical and Dental Supplies and Equipment in Storeroom; Report of

Encl: (1) Sample form of "Analysis of Standard Medical and Dental Supplies and Equipment" available for use

1. The Bureau of Medicine and Surgery is required from time to time to furnish values of standard medical and dental supplies and equipment held in the storerooms of naval hospitals and shore stations.

2. It is requested that one copy of enclosure (1) be submitted, reflecting values of standard medical and dental supplies and equipment held in storerooms as of 30 September 1949, and forwarded as soon as possible but not later than 1 November 1949. Thereafter an analysis of medical and dental supplies and equipment shall be submitted quarterly with Medical Department financial reports (Hospitals - NAVMED-569 - Others - NAVMED-E). A standard NAVMED reporting form will be distributed prior to the next reporting period.

3. Attention is invited to the fact that values to be reflected on this analysis are for standard medical and dental items only (Army-Navy Catalog of Medical Material).

4. Hospital Accounting Instructions (NAVMED-P-1296) will be revised in a future change in consonance with these instructions. C. A. Swanson

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BUMED CIRCULAR LETTER 49-139 26 October 1949

From: Chief, Bureau of Medicine and Surgery
To: All BuMed Management Control Activities

Subj: Separation of Disabled Veteran Status Employees in Reductions in Force

Encl: (1) Ltr of Chief, OIR to Chief, BuMed of 12 Oct 1949

1. A copy of a recent letter from the Chief of the Office of Industrial Relations is enclosed for the information of addressees.

2. Addressees may find it possible to be of assistance in finding jobs for disabled veterans and in facilitating the reinstatement of such employees in their own organizations. Within the limits of your present facilities, addressees are requested to lend the fullest cooperation and assistance in this matter.

H. L. Pugh

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NAVY DEPARTMENT
BUREAU OF MEDICINE AND SURGERY
WASHINGTON 25, D. C.

OFFICIAL BUSINESS

Permit No. 1048
NavMed-369 -11/49

PENALTY FOR PRIVATE USE TO AVOID PAYMENT OF POSTAGE, $300